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ORIGINAL ARTICLE

CLINICO EPIDEMIOLOGICAL AND BIOCHEMICAL PROFILE OF PATIENTS WITH MELASMA

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ABSTRACT: BACKGROUND: The prevalence of melasma has been found to be 40% in females and 20% in males in Southeast Asian population. Heredity, exposure to sunlight, cosmetics eliciting phototoxic mechanisms, various hormones, pregnancy, and oral contraceptive pill usage are the factors that may influence the causation of melasma. **AIMS AND OBJECTIVES:** To study the clinico epidemiological and biochemical profile of patients with melasma. **SETTINGS AND DESIGN:** A cross sectional descriptive study was done in 30 patients with clinical diagnosis of melasma from June 2011 to June 2012. **MATERIALS AND METHODS:** Female patients above 18 years of age were included in the study. Patients with exogenous ochronosis and males were excluded from the study. Detailed clinical history was taken. Biochemical profile which included serum estradiol, progesterone, testosterone, leutinizing hormone (LH), follicle stimulating hormone (FSH), cortisol, adrenocorticotrophic hormone (ACTH), Tri-iodothyronine (T3), thyroxine (T4) and thyroid stimulating hormone (TSH) was done. **STATISTICAL ANALYSIS:** For all the statistical analysis SPSS statistical software, version 16.0 for windows (SPSS Inc, Chicago, IL, USA) was used. Chi-square test was used for statistical significance. In all instances, $p \leq 0.05$ was taken as statistically significant. **RESULTS:** Melasma was found to be more common in 40- 50 years age group (46%), with a positive family history in 53.33%. Summer exacerbation was found in 80%. Positive correlation with pregnancy was found in 33.3% and with oral contraceptive pills in 46.6%. 60% of patients belonged to Fitzpatrick skin type IV. Malar pattern was found to be most common (58.3%). Thyroid abnormalities were found in 50%. Serum estradiol was low in 3 patients and progesterone was low in 2 out of 30 patients. FSH was high in 2 patients. LH, ACTH and cortisol were normal in all patients. **CONCLUSION:** Patients with Fitzpatrick skin type IV and V were more prone to develop melasma. Freckles and lentigenes were the most commonly associated dermatological finding. Thyroid disorders were the most common systemic disease associated with melasma. Thyroid imbalances have a probable effect on onset of melasma. There appears to be a complex interplay of hormonal and environmental factors that predispose certain patients to develop melasma.

KEYWORDS: Clinicoepidemiological, Biochemical, Melasma.

INTRODUCTION: Melasma, a term from the Greek meaning, "a black color", or "a black spot", is a relatively common acquired symmetric hypermelanosis characterised by irregular light gray to brown macules involving the sun exposed areas having predilection for the cheeks, forehead, upper lip, nose, and chin.[1] The prevalence of melasma in Southeast Asia is reported to be 40% in females and 20% in males.[2] It is more frequently seen in darker skin types, that is, Fitzpatrick skin types IV, V and VI.[3]

While the exact etiology remains a mystery, several well known risk factors such as darker skin type, genetic predisposition, exposure to ultraviolet light, pregnancy, exogenous hormones (oral

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contraceptives and hormone replacement therapy), thyroid disorders, phototoxic medications and cosmetics exist. Ultraviolet radiation (UVR) induces melanocyte proliferation, migration and melanogenesis. In addition it can lead to the production of multiple cytokines, including interlukin-1, endothelin-1, alpha melanocyte-stimulating hormone (α-MSH), and adrenocorticotrophic hormone (ACTH) from keratinocytes, which in turn upregulate melanocyte proliferation and melanogenesis.[4]

Worsening of the disease with pregnancy, oral contraceptive use, in postmenopausal women on combination of estrogen and progesterone for osteoporosis, male patients receiving diethylstilbesterol for prostate cancer,[5,6] points to hormonal etiology of melasma. Lesional melasma skin has increased estrogen receptor expression as compared to normal skin.[7] Hormone receptors, blood vessels, sebaceous gland density and activity, phototoxicity, and antioxidants may be involved so that certain areas of the face are predisposed to develop melasma. Ovarian dysfunction, hepatic dysfunction and nutritional deficiency are also known to cause melasma.[3,8] Studies have also examined the possibility of neural and vascular component and have revealed increased nerve growth factor receptor and vascular endothelial growth factor receptors in lesional keratinocytes.[9,10]

Three clinical patterns of melasma have been defined. The centrofacial pattern is the most common and consists of lesions on the forehead, cheeks, nose, upper lip or chin. The malar pattern describes lesions primarily on the cheeks and nose. The mandibular pattern consists of lesions on the ramus of mandible. Melasma can be further classified based on wood's lamp examination as epidermal or dermal.[11] Epidermal lesions enhance whereas dermal lesions do not enhance on wood's lamp examination.

Though there is some evidence of a hormonal component in the pathogenesis of melasma, but the available data are conflicting, possibly because of the varied genetic backgrounds of the different study populations. Further research into the effects of hormones on melasma is needed.

MATERIALS AND METHODS: A cross sectional study was done in 30 patients.
Inclusion Criteria: Female patients above 18 years of age with clinical diagnosis of melasma.

Exclusion Criteria: Patients with exogenous ochronosis and males were excluded from the study.
Informed consent was obtained from all the patients included in the study. Detailed demographic and clinical history which included age of onset of melasma, duration of melasma, seasonal variation, aggravating and relieving factors, history of temporal correlation of melasma with pregnancy or oral contraceptive pills (OCP) usage, history of drug intake and family history was taken. All the patients included in the study were examined to note the fitzpatric skin type. The pattern of melasma was determined based on distribution of pigmentation. Severity of melasma was assessed by modified melasma area and severity index (MASI). Biochemical profile which included serum estradiol, progesterone, testosterone, leutinizing hormone, follicle stimulating hormone, cortisol, adrenocorticotrophic hormone, T3, T4 and TSH was done.

Ethics: The procedures followed were in accordance with the ethical standards of the institutional committee responsible on human experimentation and with the Helsinki Declaration of 1975 that was revised in 2000.

Statistics: For all the statistical analysis SPSS statistical software, version 16.0 for windows (SPSS Inc, Chicago, IL, USA) was used. Chi-square test was used for statistical significance. In all instances, $p \leq 0.05$ was taken as statistically significant.

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RESULTS: Melasma was found to be more common in 40- 50 years age group (46.46%) with 60% of patients having onset of disease in the age group of 20-40 years. Duration of melasma ranged from 6 months to 20 years with mean of 3.5 years. Family history was positive in 53.33%. All patients with age of onset between 20-30 had a positive family history (100%) while patients with age of onset between 30-40 years had 66.6% positive family history. Summer exacerbation was found in 80%. The commonly noted exacerbating factors are represented in fig. 1.

Positive correlation with pregnancy was found in 33.3% and with oral contraceptive pills in 46.6%. 60% of patients belonged to Fitzpatrick skin type IV. Malar pattern was found to be most common (58.3%) followed by centrofacial pattern (40%). Modified MASI ranged from 1.8 to 12.5, with mean -5.83, median-5.4, mode-5.4, standard deviation-2.4. Patients with earlier age of onset had severe melasma. There was a statistically significant correlation between duration of melasma and severity of melasma at 5% confidence interval. (chisquare = 118.881a, df = 77, p =.002). Upon wood's lamp examination mixed pattern was observed in all 30 patients. Associated dermatological conditions are shown in fig. 2.

Thyroid disorders were the most commonly associated systemic disease found in 50% patients.14 patients out of 30 were hypothyroid out of which 10 had clinical hypothyroidism and 4 had subclinical hypothyroidism. This was followed by hypertension and diabetes mellitus in 30% and 26.6% respectively. Fibroid uterus was observed in 16.6% patients. Correlation of pregnancy induced and oral contraceptive induced melasma with thyroid abnormalities is shown in fig. 3 and fig. 4 respectively.

Serum estradiol was low in 3 out of 30 patients with normal LH levels and not showing any significant correlation with pregnancy or OCP intake. Progesterone was low in 2 out of 30 patients not showing any significant correlation with pregnancy or OCP intake. FSH was high in 2 patients but FSH/LH ratio was maintained and LH was normal in all 30 patients, not showing any significant correlation with other hormones, pregnancy, OCP intake, age of onset or pattern of melasma. ACTH and cortisol were found to be normal in all 30 patients.

DISCUSSION: Melasma is one of the common causes of cosmetic concern in middle aged female population. Off late there has been a lot of interest in the hormonal imbalances as the cause of melasma. The mean age of presentation in our study was 39.9 years which is consistent with 38 years in a previous study conducted by Rashmi Sarkar et al.[12] In our study, positive family history was noted in 53.3% patients which is consistent with the study conducted by Athar Moin et al who reported positive family history in 54.7%.[13] Patients having positive family history had an earlier age of onset. Literature review till date has not shown any study correlating family history with the age of onset of melasma. In our study, 100% family history was noted in patients with earlier age of onset.

History of summer exacerbation was found in 80% of patients. None of the studies available in the literature have found this. Sun exposure was found to be a common exacerbating factor noted in 86% of patients. This is consistent with Guinot C, Cheffai S, et al who reported the same in 84% of patients.[14] This correlation is well explained by the fact that UVR and visible light cause peroxidation of lipids in cellular membranes, leading to generation of free radicals, which stimulate melanogenesis.

Stress as aggravating factor was observed in 53.3% patients in our study which is consistent with a previous study by Margaret songet et al who reported stress in 60% patients as an aggravating factor.[15] Cosmetics as an aggravating factor was found in 13.3% of patients in our study compared to

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a study by Sarkar et al who reported relatively low incidence of 6%.[16] 46.6% of patients in our study gave positive temporal correlation of melasma and OCP usage.

In a study conducted by Cheffai S et al only 27% of patients gave history of positive correlation of melasma with OCP usage.[14] though some of these patients had other hormonal abnormalities associated with it, oral contraceptives definitely seem to influence the onset of melasma by changing the internal hormonal milieu of the body.

In our study 33.3% of patients gave history of correlation of melasma with pregnancy. Higher incidence of 51% was noted in a study conducted by Cheffai S, et al[14] and a lower incidence of 22.4% was reported in a study by Pathak M.A et al.[15]

In our study maximum number of patients were found to have Fitzpatrick skin type 4(60%) followed by Fitzpatrick skin types 3 and 5(23.3% and 16.6% respectively) which is consistent with study conducted by Zachian T F et al (68%).[3] In our study malar pattern was found to be the most common pattern observed in 58.3% followed by centrofacial in 40%. Mandibular pattern was observed in a single patient which is consistent with a study conducted by Binayak et al where malar pattern was present in 62% patients.[17] Many other studies have reported centrofacial pattern as the most common pattern of melasma.

Severity of melasma was assessed with the help of modified MASI which ranged from 1.8 to 12.5. Severity of melasma was correlated with duration and p value was found to be 0.002, which is consistent with other studies.

Freckles and lentigenes (F&L) were the most commonly associated dermatological finding, found in 63.3% followed by dermatosis papulosis nigra (DPN) and seborrheic keratosis (SK) in 60% patients which was followed by acne vulgaris in 46.6% patients. Hirsutism (13.3%), acanthosis nigricans (AN) (16.6%) periorbital hypermelanosis (POH) (16.6%), others (10%) were the other associated findings in our study. Hassan Adalatkhah et al found that existence of some types of nevi specially the lentigenes and melanocytic nevi increase the chance of melasma.[18] Associated dermatological conditions can be attributed to the common etiological factors like sun exposure and hormonal imbalance.

Most common systemic disorder associated with melasma was thyroid abnormalities (50%) which is consistent with findings of Sheth et al and Ameneh Yazdanfar et al who stated that patients with melasma from any etiology were four times more likely to have thyroid abnormalities than the age and sex matched controls.[19] Other systemic associations were hypertension (30%), diabetes mellitus (26.6%) and fibroid uterus (16.6%). There is no other study which correlates the association of melasma with hypertension, diabetes mellitus and fibroid uterus.

Women who developed melasma during pregnancy or while taking oral contraceptives had a 70% and 69.23% incidence of thyroid abnormalities compared to 35% of those with idiopathic melasma. The results of our study are consistent with study conducted by Lutfi et al who reported 70% women who developed melasma during pregnancy or while on OCP had thyroid abnormalities compared to 39.4% with idiopathic melasma.[20]

Our study did not show any significant changes in the estradiol, testosterone, progesterone, LH, FSH, ACTH, and cortisol levels measured on 2nd day of menstrual cycle. The results of our study are consistent with a study conducted by Length Corda et al in relation to serum LH, FSH, testosterone, estradiol, and progesterone. They conducted a case control study on 13 patients in whom serum LH, FSH, testosterone, estradiol, progesterone, TSH, free T3 and free T4 were measured.

There was no significant difference in the hormone levels in the study and control groups.[21] In

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contrast to the above mentioned study in our study we found a significant correlation between hypothyroidism and melasma especially pregnancy and OCP induced melasma than idiopathic melasma.

Different studies conducted by different investigators resulted in controversial results i.e in a study conducted by Iffat Hassan et al, high follicular phase estrogen observed in a statistically significant number of patients indicates its possible influence in maintaining melasma,[22] whereas in another study conducted by Maritza Perez et al, statistically significant increased levels of LH and lower levels of serum estradiol were reported and it was proposed that these hormonal alterations may represent subclinical evidence of a mild ovarian dysfunction which may underlie the pathogenesis of idiopathic melasma.[23] Controversial results in different studies might be due to difference in genetic constituency of study populations in different studies. Probably a larger study population with hormonal level measurements in different phases of follicular cycle may be needed to know the exact role of various hormones in the etiopathogenesis of melasma.

The major limitation in our study is high cost of investigations, hormonal analysis in only one phase of menstrual cycle due to significant discomfort to the patient to get the investigations done in all the phases and absence of control group.

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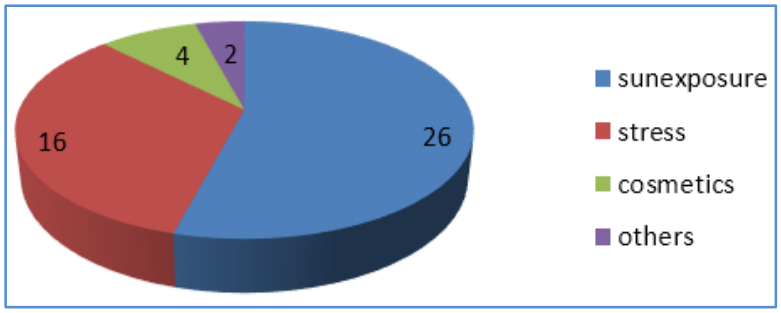

Fig. 1: Pie diagram presenting Commonly noted exacerbating factors

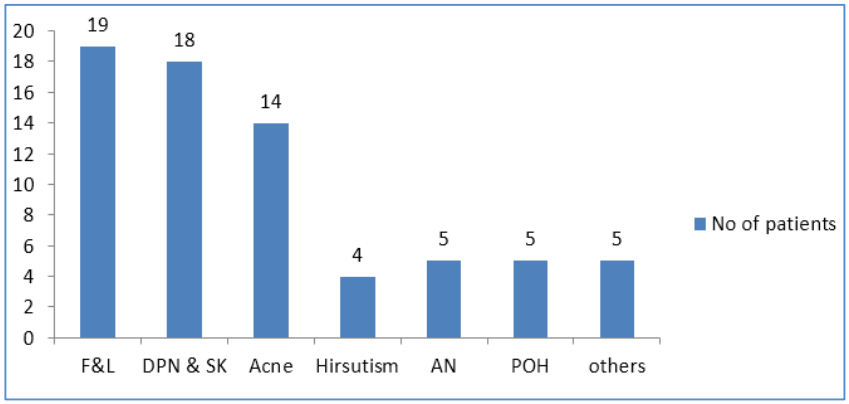

Fig. 2: Bar diagram presenting Associated dermatological conditions

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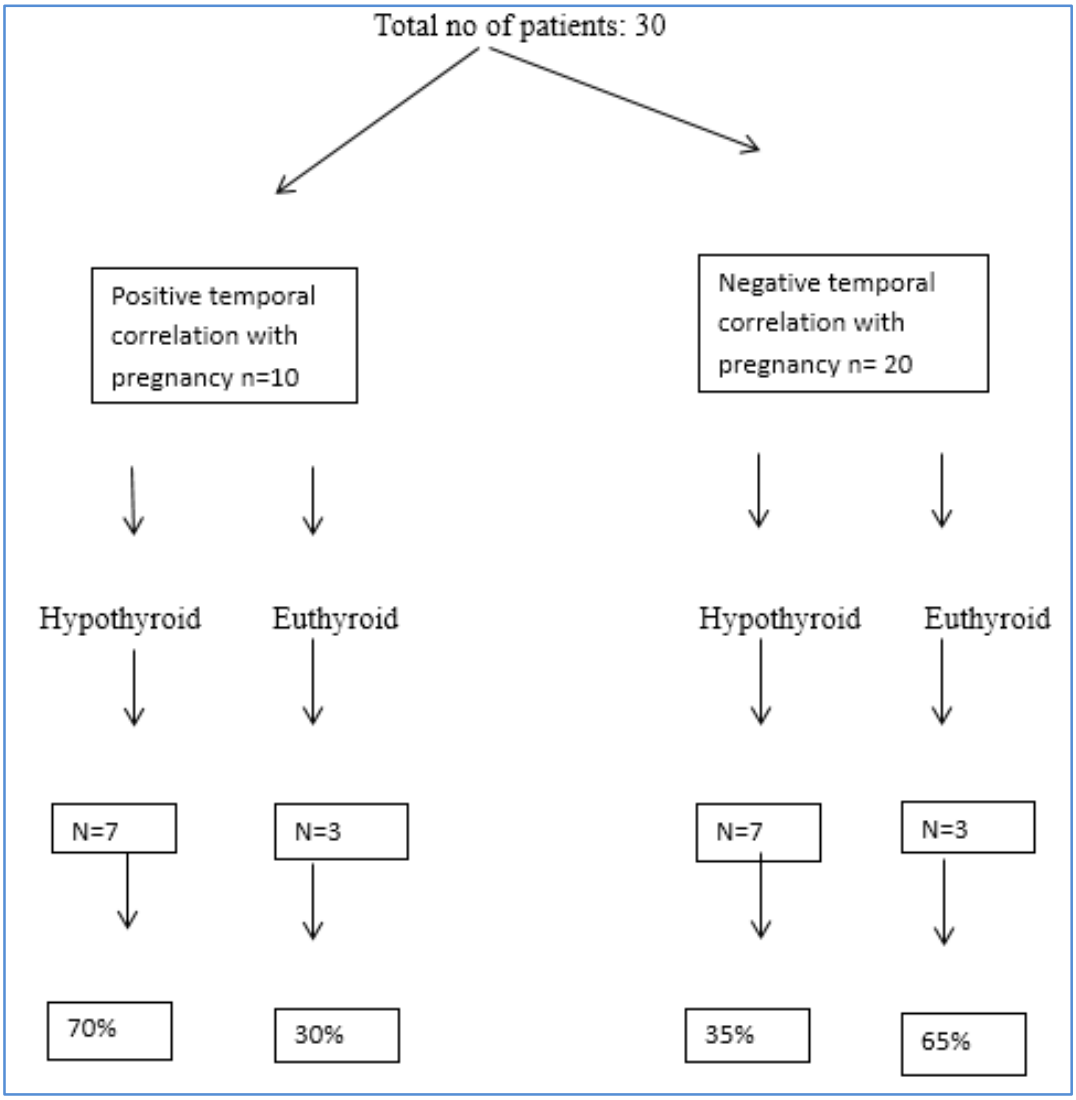

Fig. 3: Correlation of pregnancy induced melasma with associated thyroid abnormalities

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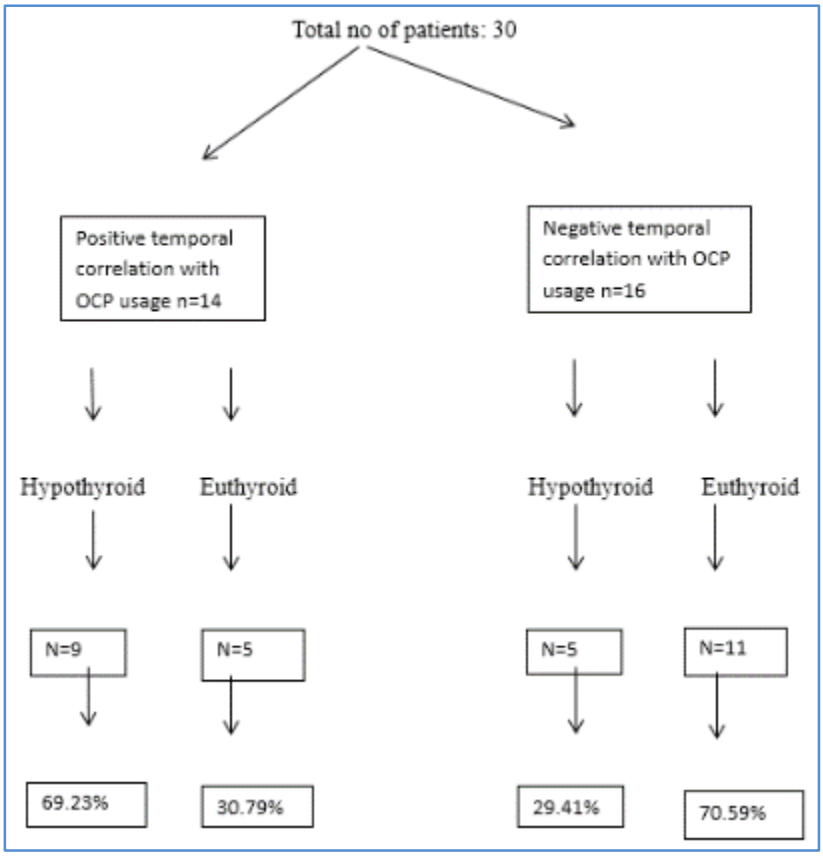

Fig. 4: Correlation of oral contraceptive induced melasma with associated thyroid abnormalities

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